

CLAIMS

1. A viral vector system comprising:
- (i) a first nucleotide sequence encoding an external guide sequence capable of binding to and effecting the cleavage by RNase P of a second nucleotide sequence, or transcription product thereof, encoding a viral polypeptide required for the assembly of viral particles; and
 - (ii) a third nucleotide sequence encoding said viral polypeptide required for the assembly of viral particles, which third nucleotide sequence has a different nucleotide sequence to the second nucleotide sequence such that the third nucleotide sequence, or transcription product thereof, is resistant to cleavage directed by the external guide sequence.
2. A system according to claim 1 further comprising at least one further first nucleotide sequence encoding a gene product capable of binding to and effecting the cleavage, directly or indirectly, of a second nucleotide sequence, or transcription product thereof, encoding a viral polypeptide required for the assembly of viral particles, wherein the gene product is selected from an external guide sequence, a ribozyme and an anti-sense ribonucleic acid.
3. A viral vector production system comprising:
- (i) a viral genome comprising at least one first nucleotide sequence encoding a gene product capable of binding to and effecting the cleavage, directly or indirectly, of a second nucleotide sequence, or transcription product thereof, encoding a viral polypeptide required for the assembly of viral particles;
 - (ii) a third nucleotide sequence encoding said viral polypeptide required for the assembly of the viral genome into viral particles, which third nucleotide sequence has a different nucleotide sequence to the second nucleotide sequence such that said third nucleotide sequence, or transcription product thereof, is resistant to cleavage directed by said gene product;
- wherein at least one of the gene products is an external guide sequence capable of binding to and effecting the cleavage by RNase P of the second nucleotide sequence.

09936572.121101

4. A system according to claim 3 wherein in addition to an external guide sequence, at least one gene product is selected from a ribozyme and an anti-sense ribonucleic acid.
5. A system according to ~~any one of claims 1 to 4~~ wherein the viral vector is a retroviral vector.
6. A system according to claim 5 wherein the retroviral vector is a lentiviral vector.
7. A system according to claim 6 wherein the lentiviral vector is an HIV vector.
8. A system according to ~~any one of claims 5 to 7~~ wherein the polypeptide required for the assembly of viral particles is selected from ~~gag, pol and env~~ proteins.
9. A system according to claim 8 wherein at least the gag and pol proteins are from a lentivirus.
10. A system according to claim 7 wherein the env protein is from a lentivirus.
11. A system according to claim 9 or 10 wherein the lentivirus is HIV.
12. A system according to any one of the preceding claims wherein the third nucleotide sequence is resistant to cleavage directed by the gene product as a result of one or more conservative alterations in the nucleotide sequence which remove cleavage sites recognised by the at least one gene product and/or binding sites for the at least one gene product
13. A system according to any one of claims 1 to 11 wherein the third nucleotide sequence is adapted to be resistant to cleavage by the at least one gene product.
14. A system according to any one of the preceding claims wherein the third nucleotide sequence is codon optimised for expression in producer cells.
15. A system according to claim 14, wherein the producer cells are mammalian cells.

SUB
B1

SUB
B2
TOTAL 121101

SUB
B3

16. A system according to any one of the preceding claims comprising a plurality of first nucleotide sequences and third nucleotide sequences as defined therein.

17. A viral particle comprising a viral vector genome as defined in any one of claims 3 to 16 and one or more third nucleotide sequences as defined in any of claims 3 to 16.

18. A viral particle produced using a viral vector production system according to any one of claims 3 to 16.

19. A method for producing a viral particle which method comprises introducing into a host cell (i) a viral genome as defined in any one of claims 3 to 16 (ii) one or more third nucleotide sequences as defined in any of claims 3 to 16 and (iii) nucleotide sequences encoding the other essential viral packaging components not encoded by the one or more third nucleotide sequences.

20. A viral particle produced by the method of claim 19.

21. A pharmaceutical composition comprising a viral particle according to claims 17, 18 or 20 together with a pharmaceutically acceptable carrier or diluent.

22. A viral system according to any one of claims 1 to 17 or a viral particle according to claims 17, 18 or 20 in treating a viral infection.

23. A viral system according to any one of claims 1 to 17 for use in a method of producing viral particles.

SUB
B4

SUB
B5

Add
B6

00036572-121101